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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,866	11/21/2000	IVO GLYNNE GUT	147-202P	2276

7590 08/11/2005  
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EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT PAPER NUMBER

1634

DATE MAILED: 08/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/555,866

Applicant(s)

GUT ET AL.

Examiner

Jeanine A. Goldberg

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-22 and 24-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 0305.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. This action is in response to the papers filed September 8, 2004 . Currently, claims 1-23 are pending. Claim 23 has been withdrawn as drawn to non-elected subject matter.

### ***Election/Restrictions***

2. Applicant's election without traverse of Group I, Claims 1-22 in the paper filed September 8, 2004 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

### ***Priority***

3. This application is a 371 of PCT/EP98/07911, filed December 4, 1998 which claims priority to EPO 97121471.3, filed December 5, 1997.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

### ***Drawings***

4. The drawings are acceptable.

### ***Claim Rejections - 35 USC § 112- Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

B) Claim 9 is indefinite over the recitation "Gene32- nucleic acids linking" because it is unclear what is Gene32. The specification teaches Gene32 is a protein binding single DNA in an unspecified way. This term appears to be arbitrary and does not appear to have any meaning established in the art or the specification. It is unclear what constitutes a Gene32 nucleic acids linking. The art teaches a T4 phage Gene32, however the art also teaches a variety of newly discovered genes which have been designated Gene32. The claim has been broadly interpreted to be any protein binding.

#### **Response to Arguments**

The response traverses the rejection. The response asserts

This argument has been considered but is not convincing because the

Thus for the reasons above and those already of record, the rejection is maintained.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

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applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-22 and Newly added Claims 24-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Van Ness et al (US 6,027,890, February 2000).

Van Ness et al. (herein referred to as Van Ness) teaches a method of gene expression analysis which involves parallel measurement of hybridization with a spectrometry. Van Ness teaches that the method includes combining a set of first tagged members with a biological sample which may contain one or more members to permit binding. The tag is correlative with a particular first member and detectable by non-fluorescent spectrometry. The bound members are separated from the non-bound members. The tag is cleaved from the first member and detected by spectrometry to detect the binding of the first member to the second member.

Van Ness teaches that any member pairs may be detected including DNA, RNA and analogues such as PNA. Van Ness teaches nucleic acid fragments with internal modification such that the base (A, T, C, or G) has been modified to add a reactive functional group (col. 36, lines 50-55)(limitations of Claims 13-14, 18). Van Ness teaches that the biomolecules may be PNA, phosphorothioates and methylphosphonates (col. 74, lines 36-37)(limitations of Claim 19).

Van Ness teaches that more than 500 different and unique tagged molecules may be utilized within a given reaction simultaneously wherein each tag is unique for a selected nucleic acid fragment, probe or first or second member and may be separately identified (col. 3, lines 30-35)(limitations of Claims 27-29).

Van Ness describes the basic structure of the invention such that a tag component is bound to a linker and then to a nucleic acid fragment (col. 5, lines 20-55). Van Ness teaches that the identification of a tag by mass spectrometry is preferable based upon its molecular mass to charge ratio (limitations of Claim 10-12). Van Ness teaches combinatorial chemistry as a means for preparing tags (limitations of Claims 26). The combinatorial libraries can be used as tags for the identification of molecule of interest. Combinatorial chemistry may be defined as the systematic and repetitive, covalent connection of a set of different "building blocks" of varying structures to each other to yield a large array of diverse molecular entities (col. 29, lines 20-30)(limitations of Claim 15-17, 22).

Van Ness teaches that a method for gene expression analysis includes in a particular embodiment that DNA is covalently immobilized to the solid support (limitations of Claim 2). Van Ness teaches that the solid supports can be nylon beads, polystyrene microbeads, glass beads (col. 47, lines 23-25)(limitations of Claim 6). The solid supports are preferentially coated with an amine-polymer such as polyethylene(imine), acrylamide, amine-dendrimers (limitations of Claim 6-7). Van Ness teaches the use of avidin-biotin technology has become important and detection of specific DNA/RNA sequence by hybridization (col. 46, lines 8-15)(limitations of Claim 8-9). The solid support is then interrogated (hybridized) with one to thousands of probes which are complementary to the gene of interest. Each probe is labeled with a cleavable mass spectrometry tag. Excess or unhybridized probe is washed away and the solid support is placed in the well of a microtiter plate. Van Ness teaches that the

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non-specifically hybridizing nucleic acids are rinsed with a solution which includes a matrix mater appropriate for spectrometry (col. 55, lines 35-37)(limitations of Claim 3-4). Van Ness teaches that the probe oligonucleotide may be denatured from the solid supports (col. 92, lines 11-15)(limitations of Claim 5). The material is mixed with alpha-cyano-4-hydroxy cinnamic acid matrix prior to mass spectrometry analysis (col. 87, lines 10-15)(limitations of Claim 20-21). The mass spectrometry tag is cleaved from the solid support and the solid support is removed from the well of sample container and the contents of the well are measured with a mass spectrometer (col. 46-47). The appearance of specific mass spectrometer tags indicate the presence of RNA in a sample and the presence of RNA in the sample and evidence that a specific gene is expressed in a given biological sample.

### **Response to Arguments**

The response traverses the rejection. The response asserts that "the main claims of the present invention relate to a method wherein the probes being used each have a distinct individual mass." This argument has been considered but is not convincing because the claims, as written, broadly encompass the including of mass tags. As specifically pointed out by the response, dependant Claim 10, encompass tags. The response asserts that Van Ness does not teach to exclude or eliminate the step of cleaving the tags from the probes, nor of the complete omission of the tags. This argument has been thoroughly reviewed, but is not found persuasive because the instant claims use open claim language and therefore encompass additional steps, including a cleavage step, for example. The response asserts that the "analysis of the

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probe, rather than the tag, is underscored by the working examples.” This argument has been thoroughly reviewed, but is not found persuasive because the claims are not exclusive of an analysis of the tag to determine the sequence of the nucleic acid. Thus for the reasons above and those already of record, the rejection is maintained.

### ***Claim Objections***

Claims 24-25 objected to because of the following informalities: Claims 24-25 appear to contain a typographical error. The claims are directed to “ration.” It appears as though this recitation should be “ratio.”

Claim 26 is objected to because of the following informalities: Claims 26 appears to contain a typographical error. Claim 26, step e refers to at least one targer. It appears as though the recitation “targer” should be target.

Appropriate correction is required.

### ***Conclusion***

7. **No claims allowable over the art.**

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within



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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) O'Donnell et al. (herein referred to as O'Donnell)(Anal. Chem. Vol. 69, pages 2438-2443, 1997) teaches a high-density, covalent attachment of DNA to silicon wafers for analysis by MALDI-TOF mass spectrometry

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



**Jeanine Goldberg**

**Patent Examiner**

August 4, 2005